

## Systolic time interval fluctuations produced by acute myocardial infarction

John T. Dowling,<sup>1</sup> Graeme Sloman,<sup>2</sup> and Cecily Urquhart<sup>3</sup>

From Cardiac Department, The Royal Melbourne Hospital, Victoria 3050, Australia

*Studies were made of serial recordings of electrocardiogram, phonocardiogram, and carotid pulse in 15 patients admitted to a coronary care unit with recent definite uncomplicated acute myocardial infarction. None of the patients received digitalis preparations, diuretics, or other drugs thought to influence myocardial performance. There was abbreviation of the electromechanical (QS<sub>2</sub>) index and left ventricular ejection time index in most patients. No significant variation in the systolic time intervals of the group were found from day-to-day measurement, and individual variations were noted to be inconsistent but considerable. The pre-ejection phase/left ventricular ejection time ratio also fluctuated but the variations were not found to be significant in the group. Assessment of variations from indices obtained in normal subjects is dependent on meticulous attention to equipment used and different observer interpretation of the onset of carotid tracing upstroke and the heart sounds on the phonocardiogram. The systolic time intervals were not found useful in the individual patients when day-to-day values were compared.*

The various phases of left ventricular contraction, recently referred to as the systolic time intervals (Weissler, Harris, and Schoenfeld, 1969), have been extensively studied by atraumatic, noninvasive techniques in normal subjects of all age groups in an endeavour to permit elucidation and evaluation of decreased myocardial performance (Frank and Kinlaw, 1962; Weissler, Harris, and White, 1963; Weissler, Harris, and Schoenfeld, 1968; Ježek, 1963; Harrison *et al.*, 1964; Harris, Schoenfeld, and Weissler, 1967; Spodick and Kumar, 1968; Toutouzas *et al.*, 1969; Willemis *et al.*, 1970; Diamant and Killip, 1970; Inoue *et al.*, 1970).

Sudden necrosis of the myocardium, as occurs in acute myocardial infarction, would be expected to alter the systolic time intervals. Toutouzas *et al.* (1969) have reported shortening of electromechanical systole (QS<sub>2</sub>) in patients with acute myocardial infarction shortly after admission to hospital, and gradual lengthening of this interval towards normal during clinical recovery. Such changes may be related to the increased urinary excretion of catecholamines in many patients in the first few postinfarction days (Wallace and Klein, 1969). Isoprenaline is known to abbreviate

the major phases of the systolic time interval (Harris *et al.*, 1967).

Diamant and Killip (1970) and Gunnar *et al.* (1970) have reported that patients, grouped by clinical or electrocardiographic means, show changes in the systolic time intervals that correlate with severity of infarction. The absolute values of measured systolic time intervals in the different groups involved a wide range. In individual patients, changes in systolic time intervals have been reported to correlate well with changes in the cardiac index after acute myocardial infarction (Schoenfeld *et al.*, 1967; Garrard, Weissler, and Dodge, 1970).

The normal ranges of absolute values of the time intervals vary when different equipment, observers, and 'normal' populations are used (Kumar and Spodick, 1970). Widespread application of the techniques used to gather this information would require either rigid, meticulous standardization of equipment and methods, or the establishment of 'normal' values by each different group of investigators. Consequently, it might be expected that assessment of day-to-day changes in the systolic time intervals after acute myocardial infarction would be of value in following left ventricular performance in individual patients. The need to depend upon the above-mentioned predicted values of the various indices would then be obviated.

Received 29 December 1970.

<sup>1</sup> In receipt of National Heart Foundation of Australia Grant-in-Aid.

<sup>2</sup> Correspondence to be addressed to Dr. G. Sloman.

<sup>3</sup> In receipt of a Parke-Davis Research Grant.

Since systolic time intervals have been found to change after administration of certain drugs, such as digitalis preparations (Weissler and Schoenfeld, 1970) and beta-receptor antagonists (Harris *et al.*, 1967; Hunt *et al.*, 1970), care must be taken to exclude patients who have received such agents when studying the specific influence of myocardial infarction on these intervals.

This study concerns patients admitted to a coronary care unit who subsequently were shown to have had acute myocardial infarction, but who did not receive, nor had received within a relevant time interval, any drugs for arrhythmias, heart failure, pain, or other purposes that may have influenced myocardial performance. Day-to-day changes were observed during each patient's stay in the coronary care unit. A patient's duration of stay and drug therapy were not influenced by the values obtained.

### Patients and method

Fifteen patients (13 men, aged 37–61 years, mean 47.6 years; 2 women aged 58 and 64 years) were considered suitable for this study. All patients were admitted to the hospital's coronary care unit with a history of chest pain, satisfied the World Health Organization (1968) criteria of acute myocardial infarction, and were initially studied within 3 days of the onset of symptoms. They were re-studied at 24-hour intervals at least once more. Measurements were made during their period of stay in the unit and, in 2 cases, after transfer to a general ward, between the hours of 9 a.m. and 12.30 p.m. All subjects were free of infarction, angina, or severe pain at least when being studied, and had received only a light breakfast or no food for 4 hours before the study. In no case had a digitalis preparation been administered for at least one week, nor had diuretics, antiarrhythmic drugs (other than lignocaine at an infusion rate of 0.8 mg – 2 mg per minute), antihypertensive drugs, or long-acting antianginal preparations been administered for at least 24 hours. Cigarette smoking was not permitted. Most of the patients had received mild hypnotics at night, and some received oral diazepam 2–5 mg intermittently. No patient received a narcotic analgesic within 6 hours of the measurements being made.

The nature of the procedure to be undertaken was explained to the patient, the blood pressure was measured, and signs of cardiac failure were looked for and recorded. Patients selected were in sinus rhythm at the time recordings were made and did not have frequent supraventricular or ventricular ectopic beats. The appearance of left bundle-branch block at any time also precluded a patient from this study. One patient had right bundle-branch block throughout the period of investigation.

Recordings were made with the patient supine or semi-recumbent, the legs being horizontal, during quiet, normal breathing. The position in

which a particular patient was placed was kept the same for successive recordings.

Simultaneous recordings of the electrocardiogram, phonocardiogram, and carotid arterial pulse tracing were used to determine the left ventricular systolic time intervals. At least 10 complexes were recorded to allow measurement from 10 consecutive cardiac cycles.

The electrocardiogram was recorded by using the standard CCU chest monitoring electrodes connected to a Sanborn 350–3200A electrocardiography preamplifier. The electrocardiograph lead (usually lead II) was that which showed most clearly the earliest component of the QRS complex. This lead was used for all subsequent tracings.

The phonocardiogram was recorded by one or two crystal microphones (New Electronic Products) positioned to record the initial high frequency components of the first and second heart sounds as clearly as possible. The sites most commonly employed were the pulmonary and/or mitral areas. The frequency ranges selected on the Sanborn 350–1700B Heart Sound preamplifier depended upon the clarity of the initial high frequency vibrations, and the 100 cps setting was usually employed.

The carotid pulse tracing was recorded using a Hewlett Packard APT-16 applanation pressure transducer connected to two DC amplifiers to allow high gain, low noise differential amplification. This transducer was attached to another Sanborn 350–3200A electrocardiograph preamplifier. The transducer (natural frequency in air 300 Hz) was hand-held at right angles to the carotid artery pulsation to give an even tracing with good demarcation of the onset of rapid pressure rise and the trough of the incisura.

The preamplifier outputs were connected directly to a Sample Electronics SE 3006 ultraviolet recorder. This instrument uses four preset galvanometers (B-450) which reflect light onto sensitized 6 in 'Oscilloscript D' (Agfa Gevaert) print-out paper and so provides a high contrast recording within a few minutes under normal ambient light conditions. Unsatisfactory recordings could quickly be discovered and discarded. The paper speed was set at 100 mm/sec and time lines were recorded at 0.1 sec or 0.01 sec. The 10 msec time lines were used as the basis of measurement. The paper speed was checked to be constant.

The electrocardiogram and carotid pulse tracings were viewed on a BWD 421 twin beam cathode ray oscilloscope, connected to the Sanborn 350 unit in parallel with the recorder.

Using 10 consecutive complexes, the following time intervals of the cardiac cycle were measured with fine calipers and an accurately calibrated rule to within 5 milliseconds:

- 1 Total electromechanical systole (QS<sub>2</sub>). The interval from the onset of ventricular depolarization to the aortic component of the second heart sound, represented by the first high frequency vibration.

2 The interval from the initial high frequency vibration of the first heart sound to the first high frequency (aortic) vibration of the second heart sound ( $S_1S_2$ ).

3 Left ventricular ejection time (LVET), measured from the onset of the rapid upstroke of the carotid pulse to the nadir of the dicrotic notch.

The averages of the above measurements were calculated from 10 consecutive cardiac cycles. Complexes which did not have clearly defined points, were ectopic in origin, or immediately followed an ectopic beat, were discarded. The heart rate was calculated from the measured duration of the 10 relevant RR intervals. The pre-ejection phase or period (PEP), from the onset of electrical activity to the beginning of left ventricular ejection, was not measured directly because of the delay in transmission of the pulse wave. It required calculation by the equation

$$PEP = QS_2 - LVET$$

The PEP is the sum of two further components, the  $QS_1$  and ICT (isovolumic contraction time):

1  $QS_1$  - from the onset of electrical activity to the first heart sound - is more easily calculated than measured directly:

$$QS_1 = QS_2 - S_1S_2$$

2 ICT (isovolumic contraction time) - is taken from the onset of the first heart sound to left ventricular ejection, and again must be calculated because of delay of transmission of the pulse wave to the neck:

$$ICT = S_1S_2 - LVET.$$

Indices were calculated from the respective average measured intervals (msec) to correct the values for heart rate using the regression equations formulated by Weissler *et al.* (1968) based on measurements made in 211 normal subjects:

$$PEP \text{ index} = PEP + 0.4 \times HR \text{ msec (men and women)}$$

$$QS_1 \text{ index} = QS_1 + 0.4 \times HR \text{ msec (men and women)}$$

$$LVET \text{ index} = LVET + 1.7 \times HR \text{ msec (men)} + LVET + 1.6 \times HR \text{ msec (women)}$$

$$QS_2 \text{ index} = QS_2 + 2.1 \times HR \text{ msec (men)} = QS_2 + 2.0 \times HR \text{ msec (women)}.$$

No index was calculated for ICT, it having been shown by Weissler *et al.* (1968) and Ježek (1963) that the ICT was independent of heart rate. The PEP/LVET ratio was calculated from respective values uncorrected for heart rate (Weissler and Garrard, 1971).

## Results

In Table 1 the patients included in this study are listed with the relevant cardiovascular histories and sites of infarction at time of investigation. The ages ranged from 37 to 64 years with a mean of 50.1 years. There were 2 women (ages 58 and 64 years) and the 13 men had a mean age of 47.6 years. The day on which each study was performed is shown,

TABLE 1 Patients with uncomplicated myocardial infarction

Case No.	Sex	Age (yr)	Relevant past cardiovascular history	Site of infarction
1	M	45	Nil	Inferior
2	M	48	Nil	Inferior
3	M	48	Angina pectoris 1 wk	Inferior
4	M	50	Acute myocardial infarction (sub-endocardial) 2 wk previously	Anterior
5	M	47	Diabetes mellitus	Inferior
6	M	37	Nil	Anteroseptal
7	M	38	Angina pectoris 2 wk	Anterior
8	M	39	Old inferior infarction	Anterior
9	M	56	Hypertension 5 yr	Anteroseptal
10	M	50	Nil	Inferior
11	M	56	Small atrial septal defect	Subendocardial
12	M	44	Nil	Anterior
13	M	61	Angina 3 yr; RBBB	Anteroseptal
14	F	68	Angina pectoris 1 wk	Anteroseptal
15	F	64	Mild hypertension	Subendocardial

and each 'day' represents a 24-hour period after the estimated time of onset of myocardial infarction. Five of the patients with transmural infarction had involvement of the inferior wall. Case 13 had right bundle-branch block throughout.

Table 2 lists the various systolic time intervals (expressed as indices for  $QS_2$ , PEP, and LVET) and the changes occurring over 24-hour periods in the 15 patients. In individual patients a 5 msec change would be considered within the limits of experimental error. In Case 4, systolic time intervals on days 1, 2, and 4 are compared but the changes between days 2 and 4 were not used in statistical analysis.

The means of the calculated indices, ICTs, and ratios for the initial and second recordings of the 15 patients are listed in Table 3. The standard deviations (using Bessel's correction) are also calculated from these absolute figures.

Table 4 shows the means of the calculated changes (from Table 1) between the first and second recordings of the group. The standard deviations of these figures are also shown.

**$QS_2$  index** The initial recordings showed the  $QS_2$  indices to vary between 479 and 539 msec, with a mean of 519.9 msec (SD 28.8). The next recordings, taken 24 hours later, showed indices ranging from 476 to 547 msec, with a mean of 517.4 msec (SD 21.6). The day-to-day changes in individual patients ranged from a fall of 51 msec to a rise of 22 msec. In the former patient (Case 5) no obvious change in ICT or PEP/LVET ratio was found, but both LVET and PEP indices fell sharply. In Case 3 the increase in LVET index was the major contributor to the in-

crease in  $QS_2$  index. An increase of 5 or more msec occurred in 4 patients, a fall in 6, and a change of less than 5 msec in the remaining 5. The mean  $QS_2$  value at the second measurement of 517.4 was 2.5 msec shorter than on day 1, and the mean values were not statistically significantly altered ( $P > 0.25$ ). Later serial measurements in 5 of these patients showed a tendency for the  $QS_2$  index to increase, rather than to decrease. The increase was most obvious in Case 14, with electrocardiographic evidence of extensive subendocardial infarction and transmural anteroseptal infarction, though the right atrial and pulmonary artery pressures remained unaltered

between the times of the first and second studies. The LVET and  $QS_2$  indices lengthened again the following day, while the PEP index shortened. Between the fourth and fifth day, no such large fluctuation occurred and she was clinically well but for the presence of a fourth heart sound.

**Pre-ejection phase index** This systolic time interval shortened in the first 24-hour period by more than 5 msec in 3 patients (Cases 5, 7, and 10) and lengthened by 5 msec or more in 5 patients. Except for Cases 3, 5, and 6, the change in PEP index was closely (within 5 msec) paralleled by change in ICT.

TABLE 2 Changes in systolic time intervals after acute myocardial infarction

Case No.	Day	ICT (msec)	$QS_1$ index (msec)	PEP index (msec)	LVET index (msec)	$QS_2$ index (msec)	PEP/LVET	$\Delta$ ICT (msec)	$\Delta$ $QS_1$ index (msec)	$\Delta$ PEP index (msec)	$\Delta$ LVET index (msec)	$\Delta$ $QS_2$ index (msec)	$\Delta$ PEP/LVET
1	1	35	76	111	370	481	0.32						
	2	37	82	119	357	476	0.38	+2	+6	+8	-13	-5	+0.06
	3	41	85	126	361	487	0.40	+4	+3	+7	+4	+11	+0.02
	4	37	82	119	381	500	0.35	-4	-3	-7	+20	+13	-0.05
2	2	42	75	117	362	479	0.35						
	3	42	82	124	365	490	0.38	0	+7	+7	+4	+11	+0.03
	4	39	84	123	368	491	0.38	-3	+2	-1	+2	+1	+0.00
3	2	46	86	132	384	516	0.39						
	3	38	96	134	404	538	0.37	-8	+10	+2	+20	+22	-0.02
	4	41	101	142	402	544	0.40	+3	+5	+8	-2	+6	+0.03
4	1	37	93	130	404	534	0.36						
	2	37	98	135	412	547	0.39						
	3	—	—	—	—	—	—						
	4	53	100	153	400	553	0.48	+16	+2	+18	-12	+6	+0.09
5	1	47	95	142	393	535	0.42						
	2	50	76	126	358	484	0.41	+3	-19	-16	-35	-51	-0.01
6	1	48	63	111	393	504	0.31						
	2	36	73	109	397	506	0.29	-12	+10	-2	+4	+2	-0.02
7	3	57	90	147	370	517	0.47						
	4	46	91	137	384	521	0.41	-11	+1	-10	+14	+4	-0.06
8	1	47	101	148	392	539	0.47						
	2	49	107	156	390	546	0.55	+2	+6	+8	-2	+7	+0.08
9	2	47	106	153	386	539	0.50						
	3	44	111	155	379	534	0.51	-3	+5	+2	-7	-5	+0.01
10	2	58	92	150	381	531	0.47						
	3	51	90	141	385	526	0.44	-7	-2	-9	+4	-5	-0.03
11	1	48	105	153	388	541	0.46						
	2	51	102	153	369	522	0.50	+3	-3	0	-19	-19	+0.04
12	2	52	84	136	386	522	0.41						
	3	54	94	148	373	521	0.50	+2	+10	+12	-13	-1	+0.09
13	2	50	88	138	380	518	0.45						
	3	50	91	141	374	515	0.49	0	+3	+3	-6	-3	+0.04
14	2	38	91	129	381	510	0.37						
	3	52	91	143	362	505	0.47	+14	0	+14	-19	-5	+0.10
	4	61	81	142	385	527	0.41	+9	-10	-1	+23	+22	-0.06
	5	64	77	141	383	524	0.41	+3	-4	-1	-2	-3	0.00
15	1	61	85	146	387	533	0.44						
	2	60	85	145	385	530	0.45	-1	0	-1	-2	-3	+0.01

The changes in PEP index in any 24-hour period ranged from a decrease of 16 msec (Case 5) to an increase of 14 msec (in Case 14). The mean change was +1.53 msec in the initial 24-hour period. The mean PEP index at the first measurement was 136.2 (SD 14.9) msec, and, at the second measurement, 137.7 (SD 24.1) msec. This difference was likewise not statistically significant.

**QS<sub>1</sub> index** The QS<sub>1</sub> index was increased by not less than 5 msec, but not more than 10 msec in 8 patients, fell in 2 patients (Cases 5 and 14), and remained unaltered in the remaining 5. The mean QS<sub>1</sub> index at the first measurement of 88.7 msec (SD 11.5) differed insignificantly ( $P > 0.5$ ) from the value obtained at the second measurement (91.3 msec, SD 10.7), and they both differed very little from the mean expected normal values (Weissler *et al.*, 1968) of 90 msec (SD 11) for men and 89 msec (SD 9) for women.

**Isovolumic contraction time** This decreased by at least 5 msec in 4 patients and increased by 14 msec in 1 patient (Case 14). The mean first-day isovolumic contraction time was 47.5 msec (SD 7.6), and the mean second-day reading was 46.5 (SD 7.2) msec. Again, there was no significant change in this systolic time interval, and its duration varied little from the expected normal value.

**Left ventricular ejection time** It can also be seen from Table 2 that the measurements of this index changed by less than 5 msec in 6 patients (Cases 2, 6, 8, 10, 13, and 15) between the first and second recordings. A later recording in one of these patients (Case 2) still showed no change. In 6 patients (Cases 1, 5, 9, 11, 12, and 14) considerable abbreviation occurred (7 to 35 msec), in one of whom (Case 11) no electrocardiographic evidence of transmural infarction was found. In Cases 1 and 14 reversal of the initial change was noted in sequential tracings on the fourth day. Cases 3, 4, and 7 had prolongation of the index (20, 8, 14 msec, respectively) between the first and second measurements, these being on the first and second day after infarction in Case 4 and one or two days later in the other 2 cases.

The first and second recordings for the entire group had means of 383.8 (SD 10.6) and 379.7 (SD 16.5) respectively, which do not differ significantly. The mean change was -4.1 msec (SD 14.2).

**Pre-ejection phase/left ventricular ejection time (PEP/LVET) ratio** This ratio,

TABLE 3 Comparison of means of first and second measurements (15 patients)

Recording		ICT	QS <sub>1</sub> index	PEP index	LVET index	QS <sub>2</sub> index	PEP/ LVET
First	Mean (msec)	47.5	88.7	136.2	383.8	519.9	0.41
	SD	7.6	11.5	14.4	10.6	28.8	0.060
Second	Mean (msec)	46.5	91.3	137.7	379.7	517.4	0.44
	SD	7.2	10.7	29.4	16.5	21.6	0.069

SD = Standard deviation with Bessel's correction.

The differences between the two days' measurements are seen to be not statistically significant (confirmed by Student's *t* test).

TABLE 4 Changes (msec) in systolic time intervals between first and second recordings in 15 patients

	ICT	QS <sub>1</sub> index	PEP index	LVET index	QS <sub>2</sub> index	PEP/ LVET
Mean change (15 patients)	+1.07	+2.60	+1.53	-4.13	-2.53	+0.023
SD (with Bessel's correction)	6.53	7.34	8.31	14.22	16.52	0.047

These variations are of no statistical significance, as confirmed by the Student's *t* test.

using values uncorrected for heart rate, showed initial changes that were not statistically significant (mean +0.02) (SD 0.047) for the group as a whole, but an increase in ratio greater than the standard deviation of 0.04 in normal subjects (Weissler *et al.*, 1969) occurred in Cases 1, 8, 12, and 14. None of these patients later developed cardiac failure, whereas Cases 2 and 9 did so but without obvious change in the ratio. In Cases 1 and 14 a decrease in ratio of 0.04 was found in subsequent tracings.

## Discussion

This study was carried out to ascertain what changes in left ventricular systolic time intervals occur in myocardial infarction, the possible influence of other factors being kept to a minimum. Presumably not all these other factors can be excluded. It has been found, for example, that patients admitted to a coronary care unit who do not develop a rise in enzyme levels or electrocardiographic evidence of infarction, may get progressive shortening of the QS<sub>2</sub> interval (Diamant and Killip, 1970). Elderly subjects have been shown to have a shorter ejection time than normal young subjects (Friedman and Davison, 1969; Willems *et al.*, 1970). The mean age of patients in our study was 50.1 years.

Digitalis preparations induce significant abbreviation of the major systolic time intervals in normal subjects (Weissler and Schoenfeld, 1970) and in patients with myocardial infarction (Bhardwaj, Schoenfeld, and Samet, 1970). Decreased venous flow, as produced by head-up tilting and venous tourniquets, has been reported to shorten the pre-ejection phase and prolong the left ventricular ejection time (Stafford, Harris, and Weissler, 1970). Thus, diuretics may influence the systolic time intervals, and no patient in this study received them during the period in which recordings were made.

Many antiarrhythmic drugs such as propranolol, procainamide, and quinidine exert a negative inotropic effect on the heart, and so may alter the relative durations of the cardiac cycle. Lignocaine, on the other hand, has been shown to have no influence on the systolic time interval in patients with acute myocardial infarction (Sinno *et al.*, 1970). A number of our patients in this study received this agent during the time of observation at an infusion rate of less than 2 mg/min.

Diurnal variation is known to produce a fall in left ventricular ejection time and  $QS_2$  in normal subjects (Weissler *et al.*, 1965). It would have been reasonable in a study such as this to compare day-to-day values with one another provided the recordings were performed at the same time each day for a particular patient. Correlations with known normal values ascertained in the mornings only, however, would be inconclusive unless the differences were gross.

The sex of the patient has a slight effect on the values obtained (Weissler *et al.*, 1968). Severe pain and therapy with potent analgesic drugs would be expected to alter the systolic time intervals, as would acute ischaemia, angina pectoris having been shown to alter acutely the apex cardiogram (Benchimol and Dimond, 1963). Vasodilator drugs such as amyl nitrite have been shown to decrease left ventricular ejection time in patients with ischaemic heart disease (Sawayama *et al.*, 1969).

From the above discussion it will be surmised that many patients entering a coronary care unit with acute infarction must be excluded from a study of this type, and that the patients suitable for sequential study are those who do not have severe infarction and do not develop major complications in the first few days.

The observation made by Toutouzas *et al.* (1969) that the  $QS_2$  interval is shortened in acute myocardial infarction was also seen in our group. The mean value was more than

one standard deviation from the mean value calculated in normal subjects by Weissler *et al.* (1968). The measurements of  $QS_2$  in our series and Weissler's are probably comparable, the onset of ventricular depolarization and the second heart sound being minimally influenced by observer error.

The day-to-day changes in  $QS_2$ , however, were not consistent and did not exceed 4 msec in 9 instances. Return towards 'normal' values was seen both early and late in the patient's stay in the coronary care unit, viz. within 48 hours of the onset of pain in Case 4, between the second and third days in Cases 2 and 3, and between the third and fourth days in Cases 1 and 14. Obvious abbreviation of the  $QS_2$  interval was observed between the first and second days only in Cases 5 and 11. In most of the patients one may assume that the major abbreviation of this interval must have occurred during the episode of pain, and not during recovery from infarction.

The patients in this study had clinically similar severity of infarction, since major complications did not develop in any of them, and none died within one month of admission. The variation in  $QS_2$  intervals was wide, and two patients (Cases 2 and 9) who developed clinical signs of cardiac failure had initial  $QS_2$  indices of 479 and 539 msec, respectively. Schoenfeld *et al.* (1967) found a poor correlation between  $QS_2$  index and cardiac index and stroke volume. Toutouzas *et al.* (1969) reported a correlation between the maximum percentage shortening of the  $QS_2$  interval and the peak level of lactic dehydrogenase, but the time of day at which studies were performed and the use of drugs, such as digitalis and antiarrhythmics, were not described.

The left ventricular ejection time and  $QS_2$  indices in this study tended to vary similarly in both direction and magnitude. Where there was dissimilarity, the pre-ejection phase index necessarily changed in the reverse direction to the left ventricular ejection time index ( $PEP \text{ index} + LVET \text{ index} = QS_2 \text{ index}$ ). For the group as a whole, the pre-ejection phase index did not change significantly from day to day. Maintenance of a normal pre-ejection phase after acute infarction has been reported elsewhere (Halpern *et al.*, 1969; Gunnar *et al.*, 1970).

The PEP/LVET changed in most patients. It increased in a 24-hour period by more than 1 SD for normal subjects ( $=0.04$ , Weissler *et al.*, 1969) in Cases 1, 8, 12, and 14, and decreased in Cases 1, 7, and 14, there being no clinical difference between their subsequent courses. Of special interest was the prolongation in pre-ejection phase index

and similar fall in left ventricular ejection time index between days 2 and 3 in Case 14. The left ventricular ejection time index promptly returned to the day 2 level on the fourth day, the  $QS_2$  index increased similarly, and these indices and the pre-ejection phase remained unaltered thereafter. This patient at no time had signs of cardiac failure other than a fourth heart sound. Case 1 had quick reversal of the fall in left ventricular ejection time index apparent between days 2 and 3, but the pre-ejection phase index fluctuated only slightly.

Determination of these two indexes relies critically on interpretation of the time of onset of the carotid upstroke which can be difficult to determine with rapid paper speeds in some patients. We have found that the time at which the rapid upward deflection occurs is most reproducible with the APT-16 transducer. Other investigators have used the beginning of carotid upstroke, which we have frequently found to be diffuse and to give a negative or inordinately short ICT. The PEP measurements reported here are therefore probably lengthened by about 5 msec and the LVET correspondingly shortened, in some instances. Comparison of these absolute values of the PEP with those of Weissler *et al.* (1968) indicates a mean difference commensurate simply with this difference in technique. As stressed above, sequential changes in the various parameters should be independent of these technical discrepancies.

The subintervals of the pre-ejection phase (the isovolumic contraction time and  $QS_2$  index) were not statistically significantly changed over the 24-hour periods. Their measurement requires consistent clear demarcation of the onset of the first heart sound, which is sometimes difficult or impossible to obtain in patients with myocardial infarction because of the appearance of loud fourth heart sounds or, for various reasons, a soft first heart sound. The isovolumic contraction time measured by this method does not include the whole of the true contraction time since the first heart sound (indicated by high frequency vibrations) begins after initial ventricular contraction, which is more clearly seen on the apex cardiogram (Spodick and Kumar, 1968; Inoue *et al.*, 1970).

This study confirms the finding that acute myocardial infarction produces some shortening of the  $QS_2$  interval, but indicates that the deviation of this interval from the 'normal' values and the day-to-day changes are not necessarily of clinical significance in a particular patient. Fluctuations in pre-ejection phase/left ventricular ejection time ratio and other

parameters did occur in individual patients, but the direction of change may alter between the first and fourth days. The isovolumic contraction time and  $QS_1$  appear to undergo the least deviation from day to day and the left ventricular ejection time and  $QS_2$  the most. Even so, where considerable changes in the latter intervals were seen, they could not be related to the patient's clinical course. All patients in this study lived for at least two months after admission to the coronary care unit.

The application of computer techniques may facilitate greatly the further elucidation and significance of subtle changes in the systolic time intervals, particularly if various safe stressful situations such as volume load or drug therapy are also carried out to unmask evidence of ventricular dysfunction.

## References

- Benchimol, A., and Dimond, E. G. (1963). The apex-cardiogram in normal older subjects and in patients with arteriosclerotic heart disease. Effect of exercise on the 'a' wave. *American Heart Journal*, **65**, 789.
- Bhardwaj, P., Schoenfeld, C. D., and Samet, P. (1970). Hemodynamic effects of digitalis in acute myocardial infarction. *Circulation*, **42**, Suppl. III, 135.
- Diamant, B., and Killip, T. (1970). Indirect assessment of left ventricular performance in acute myocardial infarction. *Circulation*, **42**, 579.
- Frank, M. N., and Kinlaw, W. B. (1962). Indirect measurement of isovolumetric contraction time and tension period in normal subjects. *American Journal of Cardiology*, **10**, 800.
- Friedman, S. A., and Davison, E. T. (1969). The phonocardiographic assessment of myocardial function in the aged. *American Heart Journal*, **78**, 752.
- Garrard, C. L., Weissler, A. M., and Dodge, H. T. (1970). The relationship of alterations in systolic time intervals to ejection fraction in patients with cardiac disease. *Circulation*, **42**, 455.
- Gunnar, R., Sinno, Z., Loeb, H., Bessinger, H., Chuquimia, R., and Rahimtoola, S. H. (1970). Left ventricular performance during first two days after acute myocardial infarction. *Circulation*, **42**, Suppl. III, 162.
- Halpern, B. L., Hodges, M., Dagenais, G. R., and Friesinger, G. C. (1969). Left ventricular pre-ejection period and ejection time in patients with acute myocardial infarction. *Circulation*, **40**, Suppl. III, 100.
- Harris, W. S., Schoenfeld, C. D., and Weissler, A. M. (1967). Effects of adrenergic receptor activation and blockade on the systolic pre-ejection period, heart rate, and arterial pressure in man. *Journal of Clinical Investigation*, **46**, 1704.
- Harrison, T. R., Dixon, K., Russell, R. O., Bidwai, P. S., and Coleman, H. N. (1964). The relation of age to the duration of contraction, ejection, and relaxation of the normal human heart. *American Heart Journal*, **67**, 189.
- Hunt, D., Sloman, G., Clark, R. M., and Hoffman, G. (1970). Effects of beta-adrenergic blockade on the systolic time intervals. *American Journal of the Medical Sciences*, **259**, 97.
- Inoue, K., Young, G. M., Grierson, A. L., Smulyan, H., and Eich, R. H. (1970). Isometric contraction

- period of the left ventricle in acute myocardial infarction. *Circulation*, **42**, 79.
- Ježek, V. (1963). Clinical value of the polygraphic tracing in the study of the sequence of events during cardiac contraction. *Cardiologia*, **43**, 298.
- Kumar, S., and Spodick, D. H. (1970). Study of the mechanical events of the left ventricle by atraumatic techniques: Comparison of methods of measurement and their significance. *American Heart Journal*, **80**, 401.
- Sawayama, T., Ochiai, M., Marumoto, S., Matsuura, T., and Niki, I. (1969). Influence of amyl nitrite inhalation on the systolic time intervals in normal subjects and in patients with ischemic heart disease. *Circulation*, **40**, 327.
- Schoenfeld, C. D., Robinson, J. L., Weissler, A. M., and Warren, J. V. (1967). The left ventricular systolic time intervals in myocardial infarction. *Clinical Research*, **15**, 411.
- Sinno, Z., Rahimtoola, S. H., Loeb, H., Chuquimia, R., Rosen, K., and Gunnar, R. (1970). Effect of lidocaine infusion on left ventricular function in acute myocardial infarction. *Circulation*, **42**, Suppl. III, 199.
- Spodick, D. H., and Kumar, S. (1968). Isovolumetric contraction period of the left ventricle. Results in a normal series and comparison of methods of calculation by atraumatic techniques. *American Heart Journal*, **76**, 498.
- Stafford, R. W., Harris, W. S., and Weissler, A. M. (1970). Left ventricular systolic time intervals as indices of postural circulatory stress in man. *Circulation*, **41**, 485.
- Toutouzas, P., Gupta, D., Samson, R., and Shillingford, J. (1969). Q-second sound interval in acute myocardial infarction. *British Heart Journal*, **31**, 462.
- Wallace, A. G., and Klein, R. F. (1969). Editorial. Role of catecholamines in acute myocardial infarction. *American Journal of the Medical Sciences*, **258**, 139.
- Weissler, A. M., and Garrard, C. L. (1971). Systolic time intervals in cardiac disease. *Modern Concepts of Cardiovascular Disease*, **40**, 1.
- Weissler, A. M., Harris, W. S., and Schoenfeld, C. D. (1968). Systolic time intervals in heart failure in man. *Circulation*, **37**, 149.
- Weissler, A. M., Harris, W. M., and Schoenfeld, C. D. (1969). Bedside technics for the evaluation of ventricular function in man. *American Journal of Cardiology*, **23**, 577.
- Weissler, A. M., Harris, L. C., and White, G. D. (1963). Left ventricular ejection time index in man. *Journal of Applied Physiology*, **18**, 919.
- Weissler, A. M., Kamen, A. R., Bornstein, R. S., Schoenfeld, C. D., and Cohen, S. (1965). The effect of deslanoside on the duration of the phases of ventricular systole in man. *American Journal of Cardiology*, **15**, 153.
- Weissler, A. M., and Schoenfeld, C. D. (1970). Effect of digitalis on systolic time intervals in heart failure. *American Journal of the Medical Sciences*, **259**, 4.
- Willems, J. L., Roelandt, J., De Geest, H., Kesteloot, H., and Joossens, J. V. (1970). The left ventricular ejection time in elderly subjects. *Circulation*, **42**, 37.
- World Health Organization, Regional Office for Europe (1968). *Ischaemic Heart Disease Registers: Report on a Working Group*. Copenhagen.